

Application No.: 09/719,889

2 Docket No.: 577122000200 / 30347USP00

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows.

This listing of claims will replace all prior versions, and listing, of claims in the application:

1. (currently amended) A biomolecular solder comprising a proteinaceous substance made by a method comprising
 - (b) providing a composition comprising a proteinaceous substance in a solvent; and
 - (b) pre-denaturing the proteinaceous substance before placing the composition in situ by at least partially denaturing the proteinaceous substance while moist with the solvent such that at least a portion of the proteinaceous substance bonds together and, (c) shaping the proteinaceous substance, wherein the solder is shaped before, during or after the denaturing of step (b), or a combination thereof, and, when shaped, the final shape of the solder is essentially maintained and the solubility of the proteinaceous substance is reduced in a physiological fluid at body temperature.
2. (previously presented) A solder according to claim 1 wherein the proteinaceous substance comprises a protein.
3. (currently amended) A solder according to claim 2 wherein the protein comprises is any one of an albumin, a collagen, an elastin, a fibrinogen, or any combination thereof.
4. (previously presented) A solder according to claim 1, further comprising a dye.
5. (currently amended) A solder according to claim 4 wherein the dye comprises an indocyanine green, a methylene blue or a fluorescein isothiocyanate or any combination thereof.
6. (previously presented) A solder according to claim 1, further comprising an adjuvant.

sd-227298

Application No.: 09/719,889

3 Docket No.: 577122000200 / 30347USP00

7. (currently amended) A solder according to claim 1 further comprising 6 wherein the adjuvant is selected from the group consisting of a growth factor, a sodium hyaluronate, a hormone and an anti-coagulant.

8. (previously presented) A solder according to claim 1 further comprising a material for improving the strength of the solder.

9. (previously presented) A solder according to claim 8 wherein the material comprises a polytetrafluoroethylene fibre or a ceramic fibre.

10. (currently amended) A kit comprising a biomolecular solder according to claim 1 any one of claims 1 to 9.

11. (currently amended) A method of preparing a biomolecular solder *ex vivo*, the method comprising:

(a) providing a composition biomolecular solder comprising a proteinaceous substance and a solvent;

(b) shaping the composition solder into a desired shape, wherein the composition solder is shaped before, during or after the pre-denaturing denaturing of step (c), or a combination thereof; and

(c) pre-denaturing denaturing the proteinaceous substance before placing the composition in situ by at least partially denaturing the proteinaceous substance while the composition solder is moist such that at least a portion of the proteinaceous substance bonds together, thereby preparing a biomolecular solder and the desired shape of the solder is essentially maintained and the solubility of the proteinaceous substance is reduced in a physiological fluid at body temperature.

sd-227298

Application No.: 09/719,889

4 Docket No.: 577122000200 / 30347USP00

12. (currently amended) A method according to claim 11 wherein the proteinaceous substance is pre-denatured denatured by exposing the solder to an energy for a time period that is sufficient to allow the energy to at least partially denature the proteinaceous substance.

13. (currently amended) A method according to claim 12 wherein the energy [[is]] comprises a thermal energy.

14. (currently amended) A method according to claim 13 [[11]] wherein the proteinaceous substance is pre-denatured denatured by heating the solder at a temperature of greater than 40°C for a time period of about 30 seconds or longer.

15. (currently amended) A method according to claim 14 [[or 32]] wherein in the pre-denaturing step the solder is heated in a hot liquid bath or in pressurized steam.

16. (currently amended) A method according to claim 11 wherein the proteinaceous substance is pre-denatured denatured by exposure exposing the solder to a denaturing agent for a time period that is sufficient to allow the denaturing agent to homogenously and completely denature the proteinaceous substance.

17-18. (canceled)

19. (currently amended) A method according to claim 11 wherein the biomolecular solder further comprises a dye for improving energy deposition.

sd-227298

Application No.: 09/719,889

5 Docket No.: 577122000200 / 30347USP00

20. (previously presented) A method according to claim 19 wherein the dye is in an amount between 0.1 to 2.5% w/w of the solder.

21. (currently amended) A method according to claim 19 [[20]] wherein the dye is mixed with the solvent, prior to mixing the solvent with the proteinaceous substance.

22. (currently amended) A method according to claim 11 wherein the pre-denaturing step further comprises comprising drying the composition solder, wherein a majority of the solvent is removed from the composition solder during the drying of the composition solder.

23. (canceled)

24. (currently amended) The [[A]] method of according to claim 11 wherein in the pre-denaturing step the composition solder is applied to a support structure before the proteinaceous substance is pre-denatured denatured.

25. (currently amended) The [[A]] method of according to claim 24 wherein the support structure is a mesh, a stiffener or a graft material.

26. (currently amended) The [[A]] method of according to claim 11 further comprising the step of sterilizing the biomolecular solder following the pre-denaturing denaturing of the proteinaceous substance.

27. (currently amended) A method of welding or joining a biological tissue together, the method comprising:

sd-227298

Application No.: 09/719,889

6 Docket No.: 577122000200 / 30347USP00

(a) applying a biomolecular solder according to claim 1 to the biological tissue to be welded or joined together; and

(b) exposing the biomolecular solder to an energy for a time sufficient to cause the solder to weld or join the biological tissue together.

28. (currently amended) The [[A]] method of according to claim 27 wherein the pre-denatured solder is moistened before application to the biological tissue.

29. (currently amended) The biomolecular [[A]] solder of according to claim 1 wherein the proteinaceous substance is denatured ex vivo such that it is essentially insoluble in the physiological fluid at body temperature.

30. (currently amended) The biomolecular [[A]] solder of according to claim 1 wherein the pre-denatured solder has been shaped from a composition comprising the proteinaceous substance in an amount of at least 40% w/w of the composition.

31. (currently amended) The biomolecular [[A]] solder of according to claim 1 wherein the proteinaceous substance comprises at least one substance selected from the group consisting of a protein, a polypeptide, a mixture of proteins, a biodegradable protein, a fibrous material, a synthetic polypeptide and analogues any combination thereof.

32. (currently amended) The [[A]] method of according to claim 11 further comprising drying the pre-denatured solder following the denaturation of the proteinaceous substance.

sd-227298

Application No.: 09/719,889

7 Docket No.: 577122000200 / 30347USP00

33. (currently amended) The [[A]] method of according to claim 11 wherein the pre-denatured solder, shaped into the predetermined shape, comprises the proteinaceous substance in an amount of at least 40% w/w or greater of the solder.

34. (currently amended) The [[A]] method of according to claim 11, wherein the solder initially comprises a proteinaceous substance in an amount in the range from 50% w/w to 80% w/w of the solder.

35. (currently amended) The [[A]] method of according to claim 33 or 34 wherein the solder initially comprises a solvent in an amount up to 60% w/w [[w/w]] of the solder.

36. (currently amended) The [[A]] method of according to claim 11 [[14]] wherein the pre-denaturing step comprises heating the solder is heated at a temperature in a range from between about 75°C to 100°C.

37. (currently amended) The [[A]] method of according to claim 36 wherein the pre-denaturing step comprises heating the solder is heated at a temperature in a range from between about 100°C to 150°C.

38. (currently amended) The [[A]] method of according to claim 16 wherein in the pre-denaturing step the denaturing agent comprises a chemical.

39. (currently amended) The [[A]] method of claim according to any one of claims 11, [[32, or 33]] wherein the proteinaceous substance comprises at least one substance selected from the group consisting of a protein, a polypeptide, a mixture of proteins, a biodegradable protein, a fibrous material, a synthetic polypeptide and analogues any combination thereof.

sd-227298

Application No.: 09/719,889

8 Docket No.: 577122000200 / 30347USP00

40. (currently amended) The [[A]] method of according to claim 39 wherein the proteinaceous substance comprises at least one substance selected from the group consisting of human albumin, bovine albumin, horse albumin, ovine albumin, rabbit albumin, rat albumin, and a combination thereof a protein and a polypeptide.

41. (currently amended) The [[A]] method of according to claim [[40]] 39, wherein the proteinaceous substance comprises at least one protein selected from the group consisting of an albumin, an elastin, a collagen and a fibrinogen.

42. (currently amended) The [[A]] method of according to claim 28 wherein the moistening of the pre-denatured solder increases flexibility of the solder.

43. (previously presented) The biomolecular solder of claim 1, wherein the solvent comprises an aqueous solvent.

44. (previously presented) The biomolecular solder of claim 43, wherein the aqueous solvent comprises water or saline.

45. (previously presented) The method of claim 11, wherein the solvent comprises an aqueous solvent.

46. (previously presented) The method of claim 45, wherein the aqueous solvent comprises water or saline.

sd-227298

Application No.: 09/719,889

9 Docket No.: 577122000200 / 30347USP00

47. (currently amended) The method of claim 11, wherein denaturing the protein *in situ* in step (e) comprises denaturing the proteinaceous substance is-denatured by exposing the solder to a laser energy.

48. (previously presented) The method of claim 47, wherein the laser is a diode laser.

49. (previously presented) The method of claim 27, wherein the biological tissue is welded together to effect a repair.

50. (currently amended) The biomolecular solder of claim 1, wherein denaturing the protein *in situ* in step (e) comprises denaturing all of the proteinaceous substance is-denatured.

51. (currently amended) The biomolecular solder of claim 1, wherein denaturing the protein *in situ* in step (e) comprises denaturing a portion of the proteinaceous substance is-denatured.

52. (currently amended) The method of claim 11, wherein denaturing the protein *in situ* in step (e) comprises denaturing all of the proteinaceous substance is-denatured.

53. (currently amended) The method of claim 11, wherein denaturing the protein *in situ* in step (e) comprises denaturing a portion of the proteinaceous substance is-denatured.

54. (currently amended) The biomolecular solder of claim 1, wherein the method of making the solder further comprises sterilizing the biomolecular solder before the step (d) placing of the pre-denatured solder *in situ*.

sd-227298

Application No.: 09/719,889

10 Docket No.: 577122000200 / 30347USP00

55. (currently amended) The biomolecular solder of claim 1, wherein the pre-denatured proteinaceous substance is shaped into a sheet, a tube, a partial tube, a strip, a patch, a hollow tube with a flanged end or a rod before the step (d) placing of the pre-denatured solder *in situ*, after the step (d) placing the pre-denatured solder *in situ*, or a combination thereof.

56. (currently amended) The method of claim 11, the desired shape comprises a sheet, a tube, a partial tube, a strip, a patch, a hollow tube with a flanged end or a rod before the step (d) placing of the pre-denatured solder *in situ*, after the step (d) placing the pre-denatured solder *in situ*, or a combination thereof.

57. (currently amended) A biomolecular solder comprising a protein comprising an albumin, an elastin, a collagen, a fibrinogen or a combination thereof, wherein the biomolecular solder is made by the method of claim 1, and the pre-denatured solder proteinaceous substance that has been at least partially denatured while moist such that the protein proteinaceous substance bonds together and, when shaped, the shape of the solder is thereby essentially maintained and the solubility of the protein proteinaceous substance is reduced in a physiological fluid at body temperature.

58. (currently amended) The biomolecular solder of claim 57, wherein the solder is shaped before pre-denaturing denaturation.

59. (currently amended) The biomolecular solder of claim 57, wherein the solder is shaped after pre-denaturing denaturation.

sd-227298

Application No.: 09/719,889

11 Docket No.: 577122000200 / 30347USP00

60. (currently amended) The biomolecular solder of claim 57, wherein the protein proteinaceous substance comprises a bovine, rabbit, ovine, rat or horse serum albumin protein.

61. (currently amended) The biomolecular solder of claim 57 [[60]], wherein the protein comprises a human [[an]] albumin, a human [[an]] elastin, a human fibrinogen, a human collagen or any combination thereof.

62. (previously presented) The biomolecular solder of claim 57, further comprising a dye for improving energy deposition into the solder when the solder is exposed to energy.

63. (previously presented) The biomolecular solder of claim 57, wherein the proteinaceous substance has been at least partially denatured while moist with a solvent.

64. (previously presented) The biomolecular solder of claim 63, wherein the solvent comprises an aqueous solvent.

65. (previously presented) The biomolecular solder of claim 64, wherein the aqueous solvent comprises water or saline.

66. (new) A biomolecular solder made by a method comprising:

- (a) providing a composition comprising a protein in a solvent;
- (b) pre-denaturing the protein before placing the composition *in situ* by at least partially denaturing the protein while moist with the solvent such that at least a portion of the protein bonds together; and,
- (c) shaping the pre-denatured protein, wherein the solder is shaped before, during or after the pre-denaturing of step (b), or a combination thereof.

sd-227298

Application No.: 09/719,889

12 Docket No.: 577122000200 / 30347USP00

67. (new) The biomolecular solder of claim 66, further comprising steps

(d) placing the pre-denatured solder *in situ*, and

(e) further denaturing the protein *in situ* such that the final shape of the *in situ*-denatured solder is essentially maintained and the solubility of the protein is reduced in a physiological fluid at body temperature.

68. (new) The biomolecular solder of claim 66, wherein the protein comprises albumin.

69. (new) The biomolecular solder of claim 68, wherein the albumin comprises human albumin, bovine albumin, ovine albumin, horse albumin, rat albumin or a mixture thereof.

70. (new) The biomolecular solder of claim 66, wherein the protein comprises collagen, elastin, fibrinogen or a combination thereof.

71. (new) The biomolecular solder of claim 66, wherein pre-denaturing the protein before placing the composition *in situ* comprises the step of steam heating or immersion into hot water.

Claim 72. (new) The biomolecular solder of claim 71, wherein the steam heating step comprises use of a temperature of between about 100°C and 150°C.

73. (new) The biomolecular solder of claim 66, wherein pre-denaturing the protein before placing the composition *in situ* comprises use of light, heat, radiation, ultrasound or chemicals.

74. (new) The biomolecular solder of claim 66, wherein the step of denaturing the protein *in situ* comprises exposing the solder to light, heat, radiation, ultrasound or chemicals.

sd-227298

Application No.: 09/719,889

13 Docket No.: 577122000200 / 30347USP00

75. (new) The biomolecular solder of claim 66, wherein the step of denaturing the protein *in situ* comprises exposing the solder to a laser energy.

76. (new) The biomolecular solder of claim 75, wherein the laser energy that denatures the protein *in situ* comprises a power of about 90 mW and a wavelength of about 805 nm.

77. (new) The biomolecular solder of claim 75, wherein the laser energy that denatures the protein *in situ* comprises a spot size at the solder of about 200 μm .

78. (new) The biomolecular solder of claim 66, wherein further comprising a dye.

79. (new) The biomolecular solder of claim 78, wherein the dye comprises an indocyanine green, a methylene blue or a fluorescein isothiocyanate.

80. (new) The method of claim 27, wherein the biological tissue is a human or an animal tissue.

81. (new) The method of claim 27, wherein a blood vessel, a nerve, a pancreatic duct, a liver vessel or duct, a cystic duct, a tear duct, prostatic duct, a ureter, urethra, an epididymis, a vas deferens, a fallopian tube, a bowel, a bronchi, a gastroenterological tube or duct, a respiratory tube or duct or a brain vessel, tube or duct are welded together.

82. (new) A solder according to claim 1, wherein in step (b) the proteinaceous substance is fully denatured.

sd-227298

Application No.: 09/719,889

14 Docket No.: 577122000200 / 30347USP00

83. (new) The biomolecular solder of claim 1 wherein the composition comprises a proteinaceous substance in a concentration in a range of between about 40% w/w and 80% w/w, or between about 45% w/w and 75% w/w, of the composition.

84. (new) A biomolecular solder made by a method comprising

- (a) providing a composition comprising a proteinaceous substance in a solvent;
- (b) pre-denaturing the proteinaceous substance before placing the composition *in situ* by at least partially denaturing the proteinaceous substance while moist with the solvent such that at least a portion of the proteinaceous substance bonds together and the solubility of the proteinaceous substance is reduced in a physiological fluid at body temperature; and,
- (c) shaping the proteinaceous substance, wherein the solder is shaped before, during or after the denaturing of step (b), or a combination thereof, and, when shaped, the final shape of the solder is essentially maintained.

85. (new) A sterile biomolecular solder made by a method comprising

- (a) providing a composition comprising a proteinaceous substance in a solvent;
- (b) pre-denaturing the proteinaceous substance *ex vivo* by at least partially denaturing the proteinaceous substance while moist with the solvent such that at least a portion of the proteinaceous substance bonds together; and,
- (c) sterilizing the pre-denatured solder.

86. (new) A composition comprising a shaped proteinaceous substance and a solvent, wherein the proteinaceous substance is at least partially denatured *ex vivo* while moist with the solvent such that at least a portion of the proteinaceous substance bonds together.

87. (new) The composition of claim 86, wherein the proteinaceous substance is fully denatured.

sd-227298

Application No.: 09/719,889

15 Docket No.: 577122000200 / 30347USP00

88. (new) The composition of claim 86, wherein the protein comprises an albumin, a collagen, an elastin, a fibrinogen, or any combination thereof.

89. (new) A sterile shaped biomolecular solder comprising an at least partially cross-linked proteinaceous substance and a solvent, wherein the proteinaceous substance is at least partially cross-linked while moist with the solvent such that at least a portion of the proteinaceous substance bonds together.

90. (new) A biomolecular solder comprising an at least partially cross-linked protein and a solvent, wherein the protein comprises an albumin, a collagen, an elastin, a fibrinogen, or any combination thereof, and is at least partially cross-linked while moist with the solvent.

91. (new) A kit comprising the sterile biomolecular solder of claim 85.

92. (new) A kit comprising the sterile shaped biomolecular solder of claim 89.

93. (new) A kit comprising the biomolecular solder of claim 90.

94. (new) A kit comprising the sterile biomolecular solder of claim 85, the sterile shaped biomolecular solder of claim 89 or the biomolecular solder of claim 90, and instructions for using the solder as set forth in claim 27.

sd-227298